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SYPHILIS 1948 . . .

PUBLISHED BY COLORADO DEPARTMENT OF PUBLIC HEALTH
IN COOPERATION WITH
COLORADO STATE MEDICAL SOCIETY
and
U. S. PUBLIC HEALTH SERVICE

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CONTENTS

	PAGE
Introduction	1
Foreword	2
Case Finding	3
Diagnosis	4-6
Laboratory Tests, Techniques and Interpretations	7-12
Treatment Schedules (Protracted and Rapid)	
Primary, Secondary and Early Latent Syphilis	13-14
Late Latent Syphilis	15
Neurosyphilis	16
Congenital Syphilis	17
Syphilis in Pregnancy	18
Treatment Reactions	19
Post Treatment Observation and Indications for Retreatment	20-21
Reporting	22
Referral and Consultation	23-24
Bibliography	25

Pamphlet
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INTRODUCTION

This manual was prepared by the State Department of Public Health in cooperation with the State Medical Society and the U. S. Public Health Service for use by private physicians and clinics. It is in answer to requests for recent information on acceptable epidemiologic, diagnostic and treatment techniques in the control of syphilis.

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RECOGNITION is given to the Mississippi State Board of Health
from whose booklet we have drawn in assembling this material.

FOREWORD

It is with considerable satisfaction that the Colorado State Medical Society joins the Colorado State Department of Public Health, in sponsoring this treatise on Syphilis. In the past few years, we have been given tools which greatly augment our armamentarium against the venereal diseases; tools, which if used intelligently by us, may help us to go far toward satisfactory solution of this medical and sociological problem.

The purpose of this booklet is twofold: First, to bring to your attention certain aspects of the Syphilis problem, such as the importance of detecting new cases, and the importance of tracing contacts; and, secondly, to place in the hands of every physician the means and the methods for the modern diagnosis and treatment of Syphilis.

We commend it to you, with the sincere hope that it will find a useful place in your practice.

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CASE FINDING

Find the Cases!

In order to diagnose or treat patients we must first find the cases. This therefore is one of the most if not THE most important part of a venereal disease program. The key people to accomplish this are the private physician and public health field and clinic personnel.

These groups must:

- 1) Develop a high index of suspicion in recognizing symptoms in their daily contacts with people.
- 2) Quickly find the source of infection of each new case.
- 3) Quickly find the persons who have been infected by each new case.
- 4) Quickly and adequately treat known infected cases.

In the period between July, 1946 and July, 1947, private physicians and Public Health personnel in Colorado obtained 579 contacts out of 352 untreated primary and secondary syphilis clinic admissions. From this group of 579 contacts:

- 55 were found to have primary or secondary syphilis.
- 11 had early latent syphilis.
- 3 had late syphilis.
- 18 had an unknown stage of syphilis.
- 58 were already under treatment for syphilis prior to investigation.
- 96 were not infected.
- 338 were unable to locate.

Obtaining contact information from the syphilitic patients of private physicians is one of the major unsolved problems in the ultimate control of syphilis. The failure to discover and treat infection among these contacts leaves an unchecked source of infection in the general population. Public Health personnel will be happy to visit private physicians, acquainting them with our methods of approach and offering them this field service in their practices.

Suggestions for the stimulation of case finding in private practice:

1. Encourage infected patients to bring in their marital and extra-marital contacts.
2. Do blood tests on all expectant mothers. (State Prenatal Law: Sessions Laws of Colorado 1939, Chapter 113, House Bill 470).
3. Do routine blood tests on all patients whether hospital or home.
4. Look for genital, mucous membrane and skin lesions.
5. Do quantitative tests and physical examinations on all children of infected mothers at 1, 2, 3, 6 months, 1 year and 2 year periods.
6. Do blood tests monthly for at least 3 months with apparently non-syphilitic genital lesions or following treatment for gonorrhea.
7. Call on public health personnel in your Department of Public Health for supplemental assistance in interviewing infected persons for contacts and in supplying the field service necessary in this type of program.

DIAGNOSIS

No case of syphilis would be discovered unless someone was suspicious. It may be the patient, one of his or her friends, or it may be the physician or nurse who sees the patient. If you do not suspect syphilis, you may miss the diagnosis. If you do not make a complete examination of your patient, you may miss physical signs which should make you suspect syphilis.

The Diagnosis of Syphilis

There are four general rules which apply to the diagnosis and treatment of syphilis.

1. *Suspect* syphilis in everyone.
2. *Blood test* every patient.
3. *Prove* your diagnosis.
4. *Treat when diagnosis is proven.*

Serologic Tests for Syphilis

A positive blood test should be cause for suspecting syphilis. When performed by a competent technician, a serologic test is 99% specific and 90% sensitive.

Specificity: Of 1,000 non-syphilitic persons, not more than 10 will have a positive or doubtful blood test as a result of other disease, technical error, etc.

Sensitivity: Of 1,000 syphilitics, 900 will have a frank positive blood test. For all practical purposes, two positive blood tests mean that the patient has, or has had syphilis.

A positive blood test alone is not sufficient evidence to treat a patient. A case of syphilis which has had adequate treatment may retain a positive blood test for life.

History

Is there anything in the history which should make you suspect syphilis?

1. Is there a history of lesions—genital, oral, or cutaneous?
2. Is there a history of bubo?
3. Is there history of sexual exposure?
4. Have there been miscarriages, stillbirths, premature births, puny children, or children with positive blood tests?
5. What were the results of previous blood tests?
6. Has there been treatment? How much?
7. What is the serologic status of the sex partner?

Physical Examination

Clinical evidence of active syphilis cannot be detected without examination. This is especially important in early syphilis which may be infectious. Special attention should be paid to:

1. The genitalia.
2. The mucous membranes.
3. The lymph nodes.
4. The skin.
5. The eyes.

In late syphilis one should pay special attention to:

1. The heart.
2. The eyes.
3. The skin.
4. The reflexes.

Primary Syphilis

Suspect syphilis in *every* genital lesion, in the male or the female. Suspect syphilis in persistent oral lesions. REMEMBER:

1. The diagnosis of primary syphilis is a laboratory procedure.
2. Treat only if there is a positive darkfield examination or proven positive serology.
3. Do not treat until the diagnosis is established.
4. If you do not have the facilities for darkfield examination, refer the patient for examination to someone who has, or to the Rapid Treatment Center.
5. Do serologic follow-up for three months on every patient with apparently non-syphilitic genital lesion or with gonorrhea.

Secondary Syphilis

Suspect secondary syphilis when:

1. There are multiple genital lesions.
2. There is any type of skin rash.
3. There is a sore throat which does not respond to medical management (other than Penicillin).
4. A patient with a sore throat or a rash has a febrile reaction to an initial dose of Penicillin. (Really a Herxheimer reaction).

Secondary syphilis is a diagnosis which cannot be made without the aid of laboratory tests. There must either be a positive dark-field examination or proven positive serological test for syphilis.

Latent Syphilis

Suspect latent syphilis when there is a positive blood test and no other signs or symptoms of the disease. The diagnosis of latent syphilis is *entirely* a laboratory diagnosis. If there are any signs or symptoms of the disease present, it is not latent syphilis.

Latent syphilis is arbitrarily divided into two groups, early and late. A latent case of syphilis is said to be early if there is a history of primary or secondary lesions within four years, or in the absence of such a history, if the patient is under 25 years of age. All others are classed as late latent syphilis.

A diagnosis of latent syphilis cannot be made unless central nervous system syphilis and cardio-vascular syphilis are ruled out. These conditions can be ruled out only by careful examination of the patient, examination of the spinal fluid, and by radiographic examination of the chest.

Congenital Syphilis

Suspect congenital syphilis in every baby born of a syphilitic mother, whether or not she has been treated during her pregnancy. Diagnosis may be made on the basis of persistently positive blood tests in the baby over a period of several months, or on the basis of a rising titer of the blood tests over a period of several months. Diagnosis may also be made by darkfield examination of open lesions if present, or a combination of open lesions and a proven positive blood test.

Central Nervous System Syphilis

The diagnosis of central nervous system syphilis can be suspected, but cannot be proven without examination of the spinal fluid.

Central nervous system syphilis should be suspected in the following types of patients:

1. Every "Wassermann-fast" patient.
2. Every patient with latent syphilis.
3. Every patient with a mental disturbance.
4. Every patient with ocular palsy or loss of vision.

Classifications as to type of spinal fluid changes have been set up, but they are of chief value in estimating the prognosis of the case. It has been shown that intensive treatment with Penicillin is beneficial in neuro-syphilis. However, one should not expect too much from Penicillin. It can only arrest the process. It cannot undo permanent damage which has been done.

Cardio-vascular Syphilis

This is a killing complication of late syphilis. Rule out cardio-vascular syphilis before starting treatment for latent syphilis—a Herxheimer reaction may cause death. Suspect cardio-vascular syphilis when:

1. There is an aortic murmur.
2. There is unexplained shortness of breath on nocturnal dyspnea.

3. The aortic second sound is loud and ringing.
4. There is a precordial pain.

Late Syphilis of the Skin and Mucous Membranes

Late syphilis of the skin can imitate any skin disease from primary syphilis to carcinoma. Ten basic points in the clinical diagnosis of late cutaneous syphilis are outlined below. These are suspicion-arousers.

1. The lesions are usually few in number.
2. The distribution is not symmetrical.
3. The lesions are usually indurated.
4. The lesions are usually indolent.
5. The lesions usually form *circles, or segments of circles*.
6. The lesions usually are "punched out".
7. The lesions are destructive.
8. They tend to heal in the center or on one side and spread at the border.
9. The lesions leave a thin, atrophic, "cigarette paper" scar when they heal.
10. The scars usually have a pigmented border.

If the blood test is negative in the presence of lesions of these types, *syphilis is not ruled out*.

LABORATORY TESTS, TECHNIQUES AND INTERPRETATIONS

Darkfield Examination

A positive darkfield examination constitutes a diagnosis.

Treatment, local or systemic, often causes the disappearance of organism from lesions, sometimes for long periods.

The private physician does not often have equipment for dark-field examinations. Such tests can be made at the Rapid Treatment Center, the Weld County Health Department, the Pueblo Public Health Clinic, the Denver Health Clinic or the Central Laboratory of the Department of Public Health. Shipping such material is not too practical.

Spinal Fluid Examination

Asymptomatic Neurosyphilis

Group	Comp-fixation (Kolmer)	Cells	Total Protein
I	Negative	12	Less than 45 mg.%
		8	More than 45 mg.%
II	(A) 40000 44000	20 or less	More than 45 mg.%
III	(B) 44440	300	Less than 45 mg.%
III	4444	130	60 or more mg.%

Determination if Spinal Fluid is Positive

(Interpretation used in Denver Health Clinic and Rapid Treatment Center).

	Negative	Doubtful	Positive
1. Q. Kolmer	0000	1122 (containing 1's and 2's)	3300 (containing 3's)
2. Total Protein	Below 45 mg.%		Above 45 mg.%
3. Cell Count	Below 10 cells		Above 10 cells
4. Gold Curve	000000000000 or 0000111100	1111222211 (containing 2's)	1122332211 (containing 3's or above)

N.B. Doubtfuls are reported as "Negative" or "Positive" according to the evaluation of all four factors.

Cell Count

In central nervous system syphilis the cell count is a sensitive indication of the activity of the process. Cell counts should be done within an hour after the fluid is withdrawn. A cell count of over eight lymphocytes per cmm is abnormal. A high cell count in a syphilitic patient means neurosyphilis until proven otherwise.

Total Protein

The total protein content of the cerebro-spinal fluid tends to run parallel to the cell count in active neurosyphilitic processes. Total protein determinations should be performed soon after the fluid is withdrawn to prevent erroneous results as a consequence of bacterial contamination. Tubes are distributed by the State Central Laboratory for the collection of spinal fluid for these tests. Normal total protein content of specimens obtained from lumbar puncture should not exceed 45 milligrams/100 cc.

Serologic Tests

Serologic tests for syphilis are essentially examinations to determine the presence or absence of antibody-like substances in response to infection with *Treponema pallidum*. As in the case in any infection, a certain amount of time elapses between the moment of inoculation and the development of a positive test for the disease. When the primary sore appears the serologic test for syphilis is ordinarily negative but soon becomes positive.

The serologic test for syphilis now in use in the Colorado Department of Public Health is the Kahn test (flocculation test).

Blood tests for syphilis in modern laboratory practice fall into two additional classes:

Qualitative: A standard test performed in whole serum only which will determine the presence of positivity but not its degree. A qualitative test is principally of value as a routine aid to diagnosis.

Quantitative: The Quantitative Kahn is useful in evaluating the status of the syphilitic patient, and in the control of treatment. Just as it is important to know the titer of a patient's serum against Brucella organisms or against typhoid organisms, it is important to know the titer of the patient's serum against the antigen used in serologic tests for syphilis. A Standard serologic test shows only whether or not the patient's serum reacts with the antigen used. A quantitative test is made by using titered amounts of the patient's serum against the antigen. The serum dilutions most commonly used are as follows:

1:	2.5	1:10	1:40
1:	5	1:20	1:80

The highest dilution of serum which is positive is taken as the end point in the test. The test is read as follows:

1: 2.5 10 units 1:10 40 units 1: 40 160 units
1: 5—20 units 1:20 80 units 1: 80 320 units

By dividing the number of units by 4, one can find the dilution in which the serum was positive.

The Quantitative Kahn is of most use in the evaluation and treatment control in early syphilis. The blood test usually is positive by the 5th to 7th weeks after the disease is contracted (1-2 weeks after the development of a primary lesion). At first this test is only weakly positive, but it rapidly becomes strongly positive. By the time that secondary syphilis develops the blood test is strongly positive.

If no treatment is given it may then begin to fall, or remain stationary at the high level. If it does fall, it usually levels off at a point which is fairly high (20 Kahn units to 80 Kahn units).

When treatment is begun during the stage of the rising titer, it usually continues to rise during treatment and then falls rapidly, reaching negative or a point nearly negative by the end of 6 months. If treatment is started after the peak has been reached, the titer may fall rapidly to negative or nearly negative. This applies to primary and secondary syphilis.

In latent syphilis the titer is nearly stationary. Treatment may cause a fall in the titer in latent syphilis. This fall in titer may or may not be sustained. When a patient has had adequate treatment, a negative spinal fluid, and a stationary low titer Quantitative Kahn, no additional treatment is necessary.

The Quantitative Kahn is especially important in the diagnosis of congenital syphilis. A Quantitative Test should be done on the cord blood of the baby born of a syphilitic mother. The titer of this blood establishes a baseline for comparison with future tests. In the absence of signs and symptoms of congenital syphilis a rising or stationary titer over a period of 3 months indicates that the baby is infected. If the baby is not infected the titer drops quite rapidly and is negative, or is approaching negative by the end of 3 months.

Quantitative Kahn serologies can be obtained upon request from the Division of Laboratories of the State Department of Public Health. It is necessary to send 10 cc of blood (two tubes), and to request that a Quantitative Kahn be done. This request is made by

writing "Quantitative Kahn" in the space provided on the request slip for remarks.

It is hoped that this information will answer some of the questions which have been asked about the Quantitative Kahn.

Hemolysis of Blood Specimens: Its Causes and Prevention

Hemolysis has been defined as a dissolution of the red blood corpuscles by a release of hemoglobin into the serum, producing a reddish colored serum.

Marked hemolysis produces an opaque deep red serum that prevents an accurate serological reading. In the laboratory, such specimens which are considered unsatisfactory for use in performing sensitive serological tests are discarded and the doctor is requested to submit another specimen. This procedure is not an arbitrary one but one that contributes materially to the maintenance of an accurate, dependable laboratory service. Hemolysis may be caused by physical, chemical or bacterial factors. Extreme heat or cold or excessive shaking will affect the condition.

Traces of acids, alkalies, alcohol or drops of water used in the cleaning and sterilizing of syringes, needles, etc., and not completely removed will produce hemolysis. Blood permitted to stand at room temperature for several days and to which bacteria have been introduced, accidentally or otherwise, will effect growth of the bacteria resulting in a cloudiness of the serum and eventually cause hemolysis.

During food digestion and absorption in the body blood serum becomes cloudy with chyle. Such specimens are called "chylous" and are also considered unsatisfactory for accurate serological tests.

To avoid this type of specimen, the blood should be collected in the morning before breakfast or several hours after a meal to insure a clear serum.

In the collection of blood specimens extreme care should be practiced as well as in their handling before sending to the laboratory. Hemolyzed specimens mean not only a delay in the obtaining of the report and inconvenience to both patient and doctor, but an increased amount of work in the laboratory for the serologists, wash room facilities and shipping clerks. Any precaution taken that will prevent hemolysis should be well worth the effort.

The following suggestions should prove of practical value in preventing this condition:

1. Be sure the needle, syringe and test tube are perfectly clean and dry. If syringe or needle are *not* dry, rinse them in a physiological salt solution prior to use.
2. Collect the blood in the morning before the patient has had breakfast or just previous to other meals.
3. Remove the needle from the syringe before emptying contents into the test tube and expel contents as slowly as possi-

ble to prevent mechanical rupture of the red blood corpuscles.

4. Allow the tube containing the blood to stand in a slanted position at room temperature, with the cork inserted, until the clot has been fully formed. Store it in the refrigerator until it is ready for mailing. DO NOT place specimen near the freezing unit but store it on the bottom shelf of the refrigerator to prevent freezing.
5. Forward specimens to the laboratory by the quickest route. Samples should reach the laboratory in the shortest possible time following collection. Specimens should be taken between the first and middle part of the week and promptly sent so as NOT to reach the laboratory over the weekend or on a holiday when the laboratory is closed. Otherwise this will necessitate holding of specimens in the Denver post-office at a warm temperature.
6. If the patient's red corpuscles fragment more easily than normal, the serum may be poured off after the clot has formed and this serum sent to the laboratory. Be careful this serum does not become unnecessarily contaminated during the pouring process.

COLORADO DEPARTMENT OF PUBLIC HEALTH
DIVISION OF LABORATORIES
DENVER

A GUIDE TO THE COLLECTION OF LABORATORY SPECIMENS AND INTERPRETATION OF REPORTS

This concise guide has been prepared to aid Colorado physicians in making more efficient use of available State Laboratory services. The laboratory report should be considered only an aid in determining the final diagnosis. It merely provides additional evidence which in conjunction with the clinical findings points toward or away from a particular diagnosis. The reliability of a laboratory report is to a large extent dependent upon the care exercised in taking the specimen and in its prompt dispatch to the laboratory. For information in the collection of specimens not listed, consult the Director of your nearest State Laboratory.

DISEASE	TYPE OF EXAMINATION	SPECIMEN	HOW TO COLLECT SPECIMEN	RESULTS REPORTED	GUIDE TO INTERPRETATION
SYPHILIS (Available only from Central Laboratory, Denver)	Kahn Precipitation Test	5cc Blood	Sterile Syringe Sterile Tube	Positive	With clinical evidence of infection a diagnosis of syphilis can reasonably be made. Without clinical evidence or history, confirming repeat specimen reports are necessary to rule out possibility of false positive.
				Doubtful	Indicates need for further serological studies, unless a definite history of infection is present.
				Negative	Repeated negative reports do not always exclude syphilitic infection. A small proportion of syphilitic patients are consistently seronegative, especially in the early primary stage.
	Kahn Quantitative Test	15cc Blood	Sterile Syringe Sterile Tubes	Units Reported as Found	This information sometimes is valuable in checking the progress of syphilitic treatment.
		5cc Spinal Fluid	Sterile Syringe Sterile Tube	Units Reported as Found	
	Kahn Verification Test	15cc Blood	Sterile Syringe Sterile Tubes	Biological Positive or Luetic Positive or Negative or Inconclusive	A Biological Positive usually indicates a false positive or a positive reaction non-syphilitic in origin. A Luetic Positive usually indicates a positive reaction syphilitic in origin. A Negative report indicates a negative reaction to the test and usually accompanies negative serodiagnostic reactions. An Inconclusive report should be repeated several weeks later. This test sometimes is valuable in helping differentiate "border line" cases.
	Microscopic Darkfield	Exudate from Primary Lesion	Special Capillary Tube Submit to Laboratory immediately	Treponema pallidum Found or Not Found	The detecting of syphilitic spirochetes in exudate of primary chancre is direct evidence of syphilis infection. Negative reports may be due to too old specimen, improper collection of specimen or collection from a partially healed lesion.
	Microscopic	Smear	Glass Slide	Gram Negative Diplococci Morphologically Resembling Gonococci Found or Negative with Pus Cells or Negative	A report of gonococci found, on direct smear, is based on the finding of typical Gram negative intracellular diplococci. With the presence of clinical symptoms, failure to find the organism on direct smear has little significance. Repeat smears and send in material for culture.
	Culture	Exudate	Special Collection Tube with slanted media. Submit promptly to Laboratory	Gonococci Found or Not Found	Isolation of gonococci by cultural methods is conclusive evidence of gonorrhea. A negative report may mean the absence of the organism or that it was not isolated from this culture. If laboratory report does not confirm clinical evidence, send repeat specimen.

THE TECHNIQUE OF LUMBAR PUNCTURE¹

I. Position of the patient²

- (a) For the inexpert, the sitting position is best; landmarks are easily located; straddle a straight backed chair, place arms crosswise on top, arch back and lean head on folded arms.
- (b) For the adept, the lateral position in bed is preferable. The patient lies on either side, brings hips and shoulders both to extreme edge of bed, flexes thighs, knees bent up as far as possible towards chin, bends head down towards knees.

II. The performance of the puncture

- (a) The interspace selected is the fourth or fifth lumbar. The fourth is directly opposite the iliac crests, the fifth next below the crests.
- (b) Sterilize skin with tincture of iodine followed by 70% alcohol.
- (c) Scrub hands with brush and green soap, rinse in alcohol.

- (d) Place sterile towel about or across the hips in order to feel for the iliac crest without soiling hands.
- (e) Anesthetize skin either with 0.5-2.0% procaine injected intradermally, or by freezing with ethyl chloride, if local anesthesia is desired.
- (f) Check stylet of puncture needle—should move freely in the shaft.
- (g) Within the selected interspace, the proper landmark is the *upper border of the lower vertebra*. Introduce needle in midline, directed at an upward angle of about 10-15°.³

III. The withdrawal of fluid

- (a) About 6-10 cc of fluid for laboratory testing.
- (b) In nervous patients expedite flow by jugular compression.
- (c) Collect in three tubes, the third requiring only a few drops for an immediate cell count. (Failure to obtain fluid is due to faulty technique).

¹ Joseph Earle Moore, M.D., "The Modern Treatment of Syphilis" (second edition).

² Most important part of procedure.

³ If neatly performed there is little or no pain.

TREATMENT SCHEDULE FOR SYPHILIS

Primary, Secondary and Early Latent Syphilis

Protracted Treatment

	Mapharsen		Bismuth
Week 1)		Week 1)	
2)		2)	Bismuth Subsalicylate
3) Mapharsen intravenously		3)	0.2 gm. intramuscularly
4) .05 to .07 gm. adjusted		4)	once weekly, 5 doses.
5) to bodyweight, twice		5)	
6) weekly for 10 weeks.			
7)			
8) Total of 20 injections.			
9)			
10)			
11)		11)	
12)		12)	Bismuth
13) Omit		13)	as above
14) Mapharsen		14)	once weekly,
15) 6 weeks.		15)	6 doses.
16)		16)	
17)			
18)			
19)			
20) Mapharsen		22) Bismuth	
21) as in first course		23) as above	
22) twice weekly.		24) once weekly,	
23) Total 20 injections.		25) 5 doses.	
24)		26)	
25)			
26)			

This plan calls for a total of 40 Mapharsen and 16 Bismuth injections in a period of 26 weeks.
On the completion of treatment, early cases should be rechecked, preferably at *monthly* intervals for the first year.
Latent cases may be checked at *three month* intervals during the first year.

Thereafter, if serologically negative, both types should be rechecked at 6 month intervals for the second year, and then once a year for at least 5 years.

The serology in positive cases, as also applied to the more intensive methods, usually does not reverse to negative until 2 to 10 months after treatment has been completed.

A Quantitative test (*Kahn*) is desirable since it gives more information in following such treated cases.

Early cases should have a complete physical with each follow-up examination as banal secondary recurrences may be overlooked.

At the completion of a course of treatment of this type the patient should have a complete spinal fluid examination.

Rapid Treatments (for early syphilis)

1. 2,800,000 units Penicillin—14 days
25,000 units I.M. every 3 hours
(Crystalline "G" type)
Ars. 1 mg/k—Max. 60 mgm. on 1-4-7-10-13th day
Bis. (oil insoluble) 200 mg. on 1-7-13th day
"5-28-3"
2. 4,200,000 units Penicillin in Oil and Beeswax—14 days
300,000 units I.M. every 24 hours
"O.P.O.B. 42-0"
3. 4,200,000 units Penicillin in Oil and Beeswax—14 days
300,000 units I.M. every 24 hours
Ars. 1 mg/k max. 60 mgm. on 1-4-7-10-13th day
Bis. (oil insoluble) 200 mgm. on 1-7-13th day
"5-P.O.B. 42-3"
4. 1,800,000 units Penicillin—9 days
16,667 units I.M. every 2 hours
Ars. 1 mg/k max. 60 mgm. on 1-3-5-7-9th day
Bis. (oil insoluble) 200 mgm. on 1-5-9th day
"5-18-3"

LATE LATENT SYPHILIS

Protracted Treatment

Minimal Treatment (alternating) of Syphilis

20 Arsenicals }
20 Bismuth }

Maximal Treatment (alternating)

Spinal Fluid Examination Here

Weeks	Tri-valent Arsenical	Weeks	Heavy Metal
1} to 12}	Mapharsen	1} 2}	Bismuth
11} to 16}			Bismuth

17}
to
28}

Spinal Fluid Examination Here

35} to 46}	Mapharsen	29} to 34}	Bismuth

47}
to
52}

TOTAL 36 arms 20 hips

Treatment: In Late Syphilis not serious if no sero-reversal in 6 months.

1. 85% sero-negative in 10 years after 1 year of treatment.
2. Not any danger of Central Nervous System Syphilis if not present in beginning of treatment.

Rapid Treatment 4,200,000 units Penicillin in Oil and Beeswax—14 days
300,000 units I.M. every 24 hours

NEUROSYPHILIS

Recent studies have shown that Penicillin is the most effective single agent in the treatment of Neurosyphilis. For this reason it is recommended that as many of these cases as possible receive intensive treatment with Penicillin. If it is not possible for patients to receive intensive treatment, the following treatment is recommended.

Protracted Treatment

1. Asymptomatic

A. Neurosyphilis

- (a) Begin treatment with weekly injections of Bismuth. This may then be followed with the six (6) month Arsenic and Bismuth schedule which is outlined on page 13.

B. Spinal fluid and physical examination.

- (a) If the response has not been satisfactory the patient should be given the benefit of a course of Penicillin.

C. Indications for Penicillin treatment or for Penicillin and fever treatment.

- (a) Optic Atrophy
- (b) Interstitial Keratitis
- (c) Early Mental Deterioration
- (d) Chemo-resistant Syphilis

2. Symptomatic

The treatment is the same as for asymptomatic neurosyphilis.

Rapid Treatment

5,600,000 units Penicillin—14 days

33,334 units I.M. every 2 hours

Ars. 1 mg/k max. 60 mgm. on 1-4-7-10-13th days

Bis. (oil insoluble) 200 mgm. on 1-7-13th days

CONGENITAL SYPHILIS

Protracted Treatment

Cases of congenital syphilis (under four years) should be referred to the Colorado Rapid Treatment Center. If clinic treatment is insisted upon, the following schedule is recommended. Any case of congenital syphilis with active interstitial keratitis may be referred to the Rapid Treatment Center.

A. Treatment

Week	Treatment	Week	Treatment
1	Arsenical in one-third to one-half full dose ¹	29-40	Bismuth—note overlap
2-10	Arsenicals in full dose	41-48	Arsenical
10-19	Bismuth—note overlap	48-59	Bismuth—note overlap
20-29	Arsenical	60-65	Arsenical
		65-72	Bismuth—note overlap

¹Desirable to institute treatment even more cautiously in infants ill with active early congenital syphilis.

B. Dosage

	D o s e
	Milligrams per kilogram bodyweight Grams for II pounds (5 kilograms)
Mapharsen I.V.	0.5-1.0 .0025-.005
Neoarsphenamine I.V.	10-15 .050 -.075
Sulpharsphenamine I.M.	10-15 .050 -.075

Rapid Treatment

In infants the total dose should be at least 120,000 units of Penicillin per kilogram (2.2 pounds) bodyweight. The total duration of treatment should be at least nine days, and the interval between injections should be no more than three hours if an aqueous solution of sodium Penicillin is used and daily if Penicillin in oil and beeswax is used. From these factors the dosage given with each individual injection can be calculated. Patients over 5 years of age may be treated with a late latent rapid treatment schedule.

SYPHILIS IN PREGNANCY

Protracted Treatment

The Colorado Section of Venereal Disease Control strongly recommends that clinicians correspond with the Medical Officer in Charge of the Colorado Rapid Treatment Center as to the desirability of giving the rapid treatment to these patients. If clinic treatment is insisted upon, the following schedule is recommended.

Week of gestation .	Treatment of syphilis dis- covered in the 1st trimester of pregnancy		Treatment of syphilis dis- covered in the 2nd trimester of pregnancy		Week of gestation	Treatment of syphilis dis- covered in the 1st trimester of pregnancy		Treatment of syphilis dis- covered in the 2nd trimester of pregnancy	
1	As ¹				21	As			As
2	As				22	As			As
3	As				23	As			As
4	As				24	As			Bi
5	As				25	As	Bi		Bi
6	As				26		Bi		Bi
7	As				27		Bi		Bi
8	As				28		Bi		Bi
9	As				29		Bi		Bi
10	As	Bi ²			30		Bi		Bi
11		Bi			31		Bi	As	
12		Bi			32	As		As	
13		Bi			33	As		As	
14		Bi	As		34	As		As	
15		Bi	As		35	As		As	
16		Bi	As		36	As		As	
17		Bi	As		37	As		As	
18	As		As		38	As		As	
19	As		As		39	As		As	
20	As		As		40	As		As	

¹ A trivalent arsenical compound—Arsphenamine in 0.3 gram dose. Neoarsphenamine in 0.45 to 0.6 gram dose. Mapharsen in 0.04 to 0.06 gram dose.

² Bismuth subsalicylate suspension in oil in 0.2 gram dose.

Rapid Treatment

Depending on stage of syphilitic infection, choose one of preceding rapid treatment schedules.

TREATMENT REACTIONS—EMERGENCY MEASURES

A. Penicillin

1. Some patients will show an allergic reaction to Penicillin. This is usually urticarial in type. It is seen in about 4% of patients treated with crystalline Penicillin and in a much higher percentage of those treated with P.O.B. It is usually controlled by the administration of Benadryl, 50 mgm. every four hours for six doses and then b.i.d.
2. Herxheimer reactions may be expected in patients with primary or secondary syphilis. When such a reaction is seen the patient usually runs a fever for several hours. Symptomatic treatment is all that is required. Penicillin should not be stopped during the reaction.

B. Arsenicals

The following reactions may be seen:

1. *Pain or burning* at site of infection—an indication of drug in tissue. Stop injection, milk vein. If severe, apply hot packs locally. If no relief, 1% novocaine 5 cc injection in region of arsenical injection.
2. Nausea, vomiting or diarrhea—type treatment might need to be changed.
3. *Offensive odor or taste* during injection—hold nose or give peppermint or gum.

4. *Nitritoid reaction*—usually occurs during or immediately after injection. The patient complains of weakness and faintness, pulse is fast and thready, color pale and nausea. Stop injection, have patient lie down, loosen clothing and lower head, reassure patient. Have emergency tray ready.
5. *Skin eruption or itching*—suspend treatment—danger is development of dermatitis.
6. *Jaundice*—the giving of arsenicals should be discontinued.
7. *Blood dyscrasias*—paleness, sore throat or mouth may indicate the onset of an aplastic anemia.
8. *Tryparsamide amblyopia*—there is no need to have this treatment reaction. Patients with central nervous system syphilis are benefited more by treatment with Penicillin than by Tryparsamide.

C. Bismuth

1. *Pain radiating down leg or paroxysms of coughing*—drug might have been injected too close to sciatic nerve or into blood vessel. Stop drug.
2. *Excessive salivation, bleeding gums, sore mouth* may mean too much bismuth. While receiving bismuth instruct patient in good oral hygiene and regular visits to the dentist.

Post Treatment Observation Following the Rapid Treatments

Indications For Re-treatment

The purpose of posttreatment observation is to discover treatment failures—clinical or serologic. Patients with treatment failure of either type need retreatment. Posttreatment observation is best considered in three categories: early syphilis, late syphilis, and syphilis in pregnancy.

Early Syphilis—Acquired or Congenital

Take blood tests monthly for the first year, every three months for the second year, and if possible, annually thereafter until five years have elapsed following treatment. In most cases, four to six months or longer will be required to attain sero-negativity. Seldom will blood tests become negative at the completion of treatment or shortly afterward.

Quantitative blood tests should be used rather than qualitative. This type of test will measure the response of the patient from month to month. If the quantitative titer continues to fall, progress is satisfactory.

Serologic relapse means that the quantitative titer has shown a sustained and definite rise in two or more specimens after a preliminary fall, or after negativity has been attained. Always retreat in

cases of serologic relapse, using the same treatment schedule. Do not be misled, however, by minor fluctuations in titer which may be caused by day-to-day laboratory performance.

If, one year after treatment, the quantitative serologic tests remain positive with a titer over 1:2.5 the case can be considered seroresistant and retreatment may be indicated.

At the time the blood tests are taken, at least for the first six months, it is wise to inspect the skin, mucous membranes, and genitalia for the lesions of recurrent early syphilis. This condition is known as mucocutaneous or infectious relapse. Many times it cannot be differentiated from reinfection. In either instance, such patients always should be retreated.

In primary and secondary syphilis, spinal fluid examination should be done six months after treatment; in early latent syphilis, it should be done before, during, or as soon as possible after treatment. Spinal fluid examinations should always include cell count, total protein, and quantitative complement fixation tests. Other types of tests (colloidal gold, etc.) may be performed if desired by the physician. The Center facilities are available for lumbar puncture.

When abnormal spinal fluid findings are obtained, the patient deserves a neurologic examination before neurosyphilis treatment is started. This provides a "base line" against which to measure later the posttreatment status of the patient. (See below under Late Syphilis).

Late Syphilis—Acquired or Congenital

Perform spinal fluid examination before treatment or as soon thereafter as practicable. If negative at this time, the examination need not be repeated subsequently.

Follow-up in late syphilis relates only to the detection of clinical or spinal fluid relapse or progression. Posttreatment blood tests in late cases have no value whatever in determining whether retreatment is needed. Retreatment, of course, should be given if there is clinical or spinal fluid serologic relapse or if any lesions of late syphilis appear.

In symptomatic or asymptomatic neurosyphilis of any type, the determination of the need for retreatment is a complex matter,

and it is recommended that the general practitioner seek consultation. Spinal fluid examination should be repeated every six months.

Prenatal and Congenital Syphilis

MOTHERS: The posttreatment observation of the expectant mother does not differ from that of other patients with syphilis.

INFANTS: In infants of syphilitic mothers, regardless of whether the mother has been treated, be alert for snuffles, loss of weight, or skin lesions during the first three months following birth. After a congenital syphilitic infant has been treated, the posttreatment observation is the same as that of any other patient with syphilis.

Take blood tests on the infant at three to four months of age, or do a series of quantitative tests to determine pattern of serology.

Infants may be referred to the Rapid Treatment Center for blood testing.

REPORTING BY GENERAL PRACTITIONERS

All cases of venereal disease should be reported. A card (illustrated below) is provided by the Venereal Disease Control Section for this purpose. These may be obtained from the Denver Health Department, county health units, or from the State Department of Public Health.

It is desirable that complete information be given with every report. This is necessary to prevent the duplication of reporting which often occurs when the patient has been seen by two or more physicians over a period of time and is not reported by name.

(Front)

**CONFIDENTIAL REPORT TO
COLORADO STATE DIVISION OF PUBLIC HEALTH**

Birth date or
approximate age.....

(Last name) (First name)

Sex: Male Female Race.....
City..... County.....

TYPE OF DISEASE

SYPHILIS			
Primary <input type="checkbox"/>	Late latent <input type="checkbox"/>	Gonorrhea <input type="checkbox"/>	Chancroid <input type="checkbox"/>
Secondary <input type="checkbox"/>	Late <input type="checkbox"/>	Ophthalmia <input type="checkbox"/>	Granuloma inguinale <input type="checkbox"/>
Early latent <input type="checkbox"/>	Congenital <input type="checkbox"/>	Vulvovaginitis <input type="checkbox"/>	Lymphogranuloma <input type="checkbox"/>

HOW WAS CASE DISCOVERED?

Routine examination Prenatal Premarital Food Handler

Has the patient received previous treatment for this infection from another physician or clinic? Yes No No information

Reported by..... Date.....

Address.....
(If clinic, hospital, or State Institution, indicate name)

Check here if additional report cards are desired ROY L. CLEERE, M. D., Executive Officer.

**INSTRUCTIONS FOR REPORTING CASES OF
SYPHILIS AND GONORRHEA**

Since diagnosis involves clinical as well as laboratory examination of the patient, laboratory reports cannot serve as case reports of venereal disease. Cases of venereal disease should be reported on the attached confidential report form and forwarded in a sealed envelope. When reporting a syphilis case, the following diagnostic classification should be used:

Primary or secondary syphilis—chancre or secondary manifestation confirmed by positive darkfield or positive serologic test. Early latent syphilis—duration less than 4 years (or over age 30 if duration unknown). Late and late latent syphilis—duration over 4 years (or over age 30 if duration unknown), including late central nervous system, cardiovascular, skin, bone, or visceral syphilis. Chancroid, granuloma inguinale, lymphogranuloma venereum—clinical evidence plus adequate laboratory tests.

Report contacts to infected patients by attaching slip to card. Please give as detailed information as is possible to secure. All information is confidential. The names of the physician or patient are never revealed in the investigation process. The physician will be informed of results of investigation.

(Back)

COLORADO STATE DIVISION OF PUBLIC HEALTH

In Cooperation With U. S. Public Health Service

REQUISITION FOR FREE DRUGS

I hereby request drugs as indicated for the treatment of the patient named on the reverse side of this card.

	Dosage
Neoarsphenamine
Sulpharsphenamine
Mapharsen
Bismarsen
Bismuth subsalicylate in oil

Check if additional report cards are desired

(Physician's signature).....

(Address).....

FREE DRUGS AVAILABLE

Antisyphilitic drugs are furnished free to all Colorado licensed physicians when a morbidity report of the case is on file with the Colorado State Board of Health.

Physicians will receive 10 ampules of the arsenicals and/or one 30-cc. jar of bismuth on each order. The order may be repeated when the physician's supply is nearly used.

Drugs are available as follows:

Neoarsphenamine	0.3, 0.45, and 0.6 gram.
Sulpharsphenamine	0.2, 0.3, and 0.4 gram.
Mapharsen04 and .06 gram.
Bismarsen*2 gram.
Bismuth subsalicylate in oil	30-cc. jars.

*Bismarsen is available only for use in children.

REFERRAL AND CONSULTATION

The Colorado Rapid Treatment Center is an institution for the treatment of venereal diseases in the indigent and is under the State Department of Public Health. Years of valuable statistics on various rapid treatment schedules have been accumulated. Physicians in the Center will be happy to give assistance in planning for patients.

The Center is available to private physicians for consultation purposes and for confirmatory diagnosis or such other assistance they might desire.

1. Types of cases acceptable for treatment:

- (a) All primary and secondary (infectious) cases of syphilis.
- (b) Early latent syphilis cases (less than 4 years' duration) with no previous treatment; or, early latent syphilis inadequately treated.
- (c) Prenatal cases will be accepted preferably before the fifth month of pregnancy; can be accepted after the fifth month if the attending physician desires to take the responsibility for the travel.
- (d) Congenital syphilis (under 4 years of age) will be accepted. (See plan for admission).
- (e) Selected cases of late latent, asymptomatic neurosyphilis, late congenital syphilis and complications such as interstitial keratitis.

2. Admission routine:

- (a) Primary, secondary and early latent cases of syphilis may be referred to the Rapid Treatment Center without preliminary correspondence with Medical Officer in Charge.

(b) All other cases and conditions require previous correspondence with Medical Officer in Charge.

(c) A sealed letter containing findings, history and other pertinent information must accompany each referred patient.

3. Preferred time for admission to Rapid Treatment Center:

- (a) Only Monday, Tuesday, Wednesday, Thursday or Friday of any week unless a wait from Friday to Monday would constitute a danger to the patient or to public health.
- (b) The Rapid Treatment Center is open for admissions 24 hours a day but the preferable time is 8:30 A.M. to 4:00 P.M.

4. Payment Plan:

Up to the present time all diagnostic and treatment services have been free of charge. This arrangement might be subject to change at a future date.

5. Treatment schedules:

For primary, secondary and early latent syphilis, a combined form of treatment is being given, consisting of Penicillin every two hours for nine days, Mapharsen given in five injections on alternate days, and bismuth, three injections for the nine-day period.

For other stages of syphilis, the treatment varies with the individual case and may require as long as 15 days.

6. Follow-up Plan:

The patient is asked to inform the Center as to what physician or clinical service he intends to return after treatment. The Center sends this physician a summarized account of patient's medical findings and treatment while at the Center, and also suggestions regarding the follow-up.

If serology was positive before treatment, it is not expected to become negative immediately upon completion of treatment. There should be a drop in titer and possible negativity at about four months posttreatment. This may be delayed to six months. No further treatment should be given during this period unless there is evidence of clinical relapse or reinfection. The Medical Officer at the Center welcomes correspondence from local doctors regarding patients treated if there is some question regarding the need for further treatment.

7. Directions for referrals:

Address correspondence to:

Medical Officer in Charge
Colorado Rapid Treatment Center
Denver General Hospital
Denver 4, Colorado.

Refer patients to:

Rapid Treatment Center
Denver General Hospital
6th & Cherokee
Denver 4, Colorado.

P.S. The average length of hospitalization for syphilis is 10 to 15 days.

You are also requested to use the consultative service of the Director of the State Venereal Disease Control Section whose address is:

James R. McDowell, M.D., Director
Venereal Disease Control Section
612 Colorado Building
Denver 2, Colorado

If clinical service is desired refer to:

Denver Health Clinic
Denver General Hospital
Denver 4, Colorado

Pueblo Public Health Clinic
City Hall Basement
Pueblo, Colorado

City-County Health Unit
28 E. Boulder
Colorado Springs, Colorado

Freudenthal Health Center
723 Arizona Ave.
Trinidad, Colorado

Public Health Nursing Service
Larimer County Hospital
Ft. Collins, Colorado

Otero County Health Department
17 W. Fourth St.
La Junta, Colorado

Weld County Health Department
Courthouse
Greeley, Colorado

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National Institutes of Health
Bethesda, Maryland

